MEDICAL DEVICES CONTAINING IN-SITU GENERATED MEDICAL COMPOUNDS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention relates to medical devices containing in-situ generated medical compounds and to a method for preparing same.

2. Description of Related Art

Medical devices adapted for implant into the body to facilitate the flow of bodily fluids, to serve as vascular grafts or for other purposes have been developed. Typically, these devices include stents, catheters or cannulas, plugs, constrictors, tissue or biological encapsulants and the like.

Many of these devices used as implants are made of durable, non-degradable plastic materials such as polyurethanes, polyacrylates, silicon polymers and the like, or more preferably from biodegradable polymers which remain stable in-vivo for a period of time but eventually biodegrade in-vivo into small molecules which are removed by the body by normal elimination in urine or feces.

Typical of such biodegradable polymers include polyesters, polyanhydrides and polyorthoesters which undergo hydrolytic chain cleavage, as disclosed in U.S. Pat. No. 5,085,629; crosslinked polysaccharide hydrogel polymers as disclosed in EPA 0507604 A-2 and U.S. Pat. No. 5,057,606 and other ionically crosslinked hydrogels as disclosed in U.S. Pat. Nos. 4,941,870, 4,286,341 and 4,878,907.

EPA 0645150 A-1 describes hydrogel medical devices prepared from anionic polymers, e.g., polysaccharides such as calcium alginate or ionically crosslinked cationic polymers such as chitosan, cationic guar, cationic starch and polyethylene amine. These devices are adapted for in-vivo disintegration upon the administration of a chemical trigger material which displaces crosslinking ions.

It is often desirable to include in the formulation of such degradable or non-degradable polymer materials one or more medical compounds which have antibacterial and/or antiseptic properties or which impart radiopacity to the medical device, i.e., allow the device to be observed in-vivo by x-ray radiography. Examples of excellent antiseptic agents include silver chloride, carbonate or citrate; suitable radiopaques include barium salts such as barium sulfate and bismuth salts such as bismuth subcarbonate. Ideally, such additives have relatively low water solubility to prevent their being rapidly washed away by body fluids.

However, in many cases, these polymer compositions can not be easily manufactured due to the relative water insolubility of the medical compound additive which is to be formulated into the polymer composition, usually in an aqueous polymer medium. Formulation problems typically stem from process limitations such as viscosity (too high to mix or too low to suspend particulate fillers), thermal sensitivity of the additives to extrusion or molding process conditions used to shape the medical device, viscosity of the additives, solubility of the additives and the like.

One method used to prepare radiopaque medical devices based on polymers which are cationic salts of anionic polymers, e.g., calcium alginate, is to exchange at least a portion of the calcium ions with one or more radiopaque ions such as barium ions, as taught in commonly owned copending U.S. patent application Ser. No. 08/566,452, filed Dec. 1, 1995, the complete disclosure which is incorporated herein by reference. Such an approach may, however, introduce variables which can affect the strength and/or biodegradation properties of the treated medical device.

SUMMARY OF THE INVENTION

The present invention provides polymeric medical devices such as implants which are impregnated with a medical compound having low water solubility such as an antiseptic compound or a radiopaque compound, wherein said medical compound is formed in-situ from at least two water soluble constituents thereof.

The invention also provides a process for impregnating a medical device comprising a water absorbable polymer material with a medical compound having low water solubility comprising: a) contacting at least a portion of said device with a first aqueous solution containing a first water soluble ionizable compound dissolved therein such that the contacted portion of said device is infiltrated by said first aqueous solution; b) contacting said portion of said device with a second aqueous solution containing a second water soluble ionizable compound dissolved therein such that said contacted portion of said device is also infiltrated by said second aqueous solution; said water soluble compounds characterized by the fact that the ions thereof react after contact to form said medical compound having low water solubility within said device.

DETAILED DESCRIPTION OF THE INVENTION

Suitable polymer materials which may be used to fabricate the medical devices of this invention are either non-porous materials which are capable of swelling in and absorbing aqueous solutions such that the aqueous solution can infiltrate the polymer matrix, or porous polymer structures which permit infiltration of the aqueous solution through the pores. Examples of polymer materials which may be used include natural or synthetic polymers or copolymers. The polymer may be an ionically or covalently crosslinked hydrogel, or a non-crosslinked material.

The ionically crosslinkable polymers from which the medical device may be fabricated may be anionic or cationic in nature and may include but are not limited to carboxylic, sulfate, and amine functionalized polymers. Suitable such polymers include polyacrylic acid, polymethacrylic acid, polyethylene amine, polysaccharides such as alginic acid, pectinic acid, carboxymethyl cellulose, hyaluronic acid, heparin, chitosan, carboxymethyl chitosan, carboxymethyl starch, carboxymethyl dextran, heparin sulfate, chondroitin sulfate, cationic guar, cationic starch, and their salts. Preferred ionically crosslinkable polymers are alginic acid, pectinic acid, carboxymethyl cellulose, hyaluronic acid, chitosan, and their salts. Most preferred ionically crosslinkable polymers are alginic acid, pectinic acid, and hyaluronic acid and their salts. Among the ionically crosslinkable cationic polymers that may be employed are chitosan, cationic guar, cationic starch and polyethylene amine.

The crosslinking ions may be anions or cations. Appropriate crosslinking ions include but are not limited to cations comprising an ion selected from the group consisting of calcium, magnesium, barium, strontium, boron, beryllium, aluminum, iron, copper, cobalt, lead and silver ions. Anions may be selected from the group consisting of phosphate, citrate, borate, succinate, maleate, adipate and oxalate ions. More broadly, the anions are derived from polybasic organic or inorganic acids. Preferred crosslinking cations are calcium, iron, and barium ions. The most preferred crosslinking cations are calcium and barium ions. The most preferred crosslinking anion is phosphate.